

Serial No. 08/455,975

IN THE SPECIFICATION:

Applicants herewith submit a Substitute Specification which incorporates the changes made with the Preliminary Amendment filed May 31, 1995. The following amendments to the specification and Figures refer to the page numbers in the Substitute Specification.

At page 1, before line 1, please cancel all prior application data inserted in previous amendments and insert the following:

\* \* \*

--This application is a divisional application of application Serial No. 08/106,775, filed August 16, 1993, abandoned, which is a continuation of application Serial No. 07/780,847, filed October 23, 1991, abandoned, which is a continuation of application Serial No. 07/304,281, filed January 31, 1989, abandoned.--

Page 3, line 25, delete "FGF-5";

Page 4, line 28, delete "cells" and substitute therefor --tissue--;

Page 5, line 27, delete "FGF-5";

Page 8, line 38, delete the second recitation of "KGF or";

Page 9, line 6, delete "I-"; delete "heparin-Sepharose...NaCl." and insert the figure legend from drawing sheet 3/16 (page 55);

line 11, delete "I-" and insert --A, 2B and 2C--;

delete lines 14-23 and insert the figure legend from drawing sheet 5/16 (page 57);

line 24, delete "I-";

line 25, delete "sieving chromatography... bioassay." and insert figure legend from drawing sheet 6/16 (page 58);

line 29, delete "I-"; delete "comparison of...factors." and insert figure legend from drawing sheet 7/16 (page 59);

line 32, delete "I-"; delete "comparisons- of growth...factors." and insert figure legend from drawing sheet 8/16 (page 60);

delete lines 35-38.

Page 10, delete lines 1-14 and insert --Fig. 6 outlines a schematic representation of human KGF cDNA clones. Overlapping pCEV9 clones 32 and 49, used in sequence determination, are shown above a diagram of the complete structure in which untranslated regions are depicted by a line and the coding sequence is boxed. The hatched region denotes sequences of the signal peptide. Selected restriction sites are indicated.

Fig. 7 documents the KGF cDNA nucleotide and predicted amino acid sequences. Nucleotides are numbered on the left; amino acids are numbered throughout. The N-terminal peptide sequence derived from purified KGF is underlined. The hydrophobic N-terminal domain is italicized. The potential asparagine-linked glycosylation site is overlined. The variant polyadenylation signals, AATTAA and AATACA, close to the 3' end of the RNA, are boxed.

Fig. 8 shows identification of KGF mRNAs by Northern blot analysis. Lanes a and c, poly(A)-selected M426 RNA; lanes b and d, total cellular M426 RNA. Filters

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were hybridized with a <sup>32</sup>P-labeled 695 bp *Bam*HI/*Bcl*II fragment from clone 32 (Probe A, Fig. 6), lanes a and b, or a 541 bp *Apa*I/*Eco*RI fragment from clone 49 (Probe B, Fig. 6), lanes c and d.--;

line 15, delete "II-2" and insert --9--;

line 17, delete "sharp" and insert --share--;

line 18, after "homology" insert --(shaded boxes)--; after "sequences" insert --(hatched boxes)--;

line 19, after "residues" insert --(positions labeled with a "C")--;

line 20, delete "II-3" and insert --10--;  
delete "(Northern blot)...cell lines." and insert the figure legend from drawing sheet 16/16 (page 68).

line 22, delete "the predominant" and substitute therefor --a single--;

line 23, delete "stromal" and substitute therefor --human embryonic lung--;

line 24, delete "but was not detected in the epithelial cell lines" and substitute therefor --and from adult skin fibroblasts, while no transcript was detected in the (B5/589) epithelial or (HA 83) glial cell lines or in primary cultures of human saphenous vein endothelial cells--

Page 12, line 16, delete "I-".

Page 13, line 24, delete "I-".

Page 14, line 27, delete "II-1A" and insert --6--;

line 33, delete "II-B" and insert --7--;

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line 39, delete "FGF-5".

Page 16, line 16, delete "II-1" and insert --7--.

line 13, delete "46" and substitute therefor "about 40";

line 17, delete "116" and substitute therefor "about 140";

line 21, delete "its activity is enhanced by" and substitute therefor --lacks susceptibility to".

Page 18, line 29, delete "NH<sub>2</sub>" and insert --N--.

Page 19, lines 28-29, delete "plus an R at its C-terminus"

line 30, delete "II-1" and insert --7--.

Page 26, line 14, delete "I-";

line 34, delete "I-2" and insert --2A--;

line 38, delete "I-".

Page 27, line 1, delete "I-";

line 7, delete "I-";

line 10, delete "I-";

line 17, after "." insert Table 1 from drawing sheet 1/16;

line 21, delete "I-" and insert --A-2C--;

line 25, delete "I-";

line 39, delete "I-".

Page 28, line 9, delete "I-";

line 14, delete "I-";

line 25, delete "I-";

line 33, delete "I-";

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line 38, after "." insert Table 2 from drawing sheet 2/16.

Page 32, line 18, delete "NH<sub>2</sub>" and insert --N--.

line 24, delete "FGF-5".

Page 34, line 5, delete "II-1" and insert --7--;

line 17, delete "the conditioned medium of human--fibroblast" and substitute therefor --human epithelial--.

Page 36, line 8, delete "reference II-3" and insert --Rubin et al., Proc. Natl. Acad. Sci. USA 86: 802-806 (1989)--.

Page 37, line 4, delete "II-1A" and insert --6--;

line 9, delete "II-1B" and insert --7--;

line 25, delete "NH<sub>2</sub>" and insert --N--;

line 38, delete "FGF-5".

Page 38, line 5, delete "II-1A" and insert --6--;

line 6, delete "II-1C" and insert --8--;

line 13, delete "II-1A" and insert --6--;

delete "II-1C" and insert --8--;

line 22, delete "II-3" and insert --10--;

line 39, delete "II-3" and insert --10--.

Page 39, line 7, delete "II-3" and insert --10--;

line 12, delete "II-21, II-22" and insert -- Schreiber et al., Proc. Natl. Acad. Sci. USA 82: 6138-6142 (1985), Gospodarwizc et al., J. Cell Physiol. 128: 475-485 (1986)--;

line 14, delete "II-22" and insert --Gospodarwizc et al., supra.--

line 20, delete "II-1" and insert --3--;

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line 24, after "." insert Table 3 from drawing sheet 9/16 (page 61).

Page 40, line 9, delete "II-1" and insert --7--;  
line 12, delete "was not identified" and substitute therefor --appeared to be arg--.

Page 42, line 9, delete "SauI" and substitute therefor  
--Sau3A--;

line 10, delete "CCTGAGG" and substitute therefor --GATC--;

line 12, delete "II-1" and insert --7--;  
line 14, delete "37 (Phe), 38 (leu) and 39 (arg)" and substitute therefor --39(arg) and 40--.

Page 43, line 32, delete "FGF-5 and hst are transforming genes originally detected by DNA-mediated gene transfer" and substitute therefor --The hst gene was identified as a transforming gene from a human stomach tumor (Taira et al., *Proc. Natl. Acad. Sci. USA* 84: 2980-2984(1987), adjacent normal stomach tissue (Yoshida et al., *Proc. Natl. Acad. Sci. USA* 84: 7305-7309 (1987), and from Kaposi's sarcoma (Delli-Bovi et al., *Proc. Natl. Acad. Sci. USA* 84: 5660-5664 (1987), by standard NIH/3T3 transfection assays--.

Page 44, line 6, delete "FGF-5";

line 31, delete "II-2" and insert --9--.

Page 45, line 4, delete "II-2" and insert --9--;

line 11, delete "II-1B" and insert --7--;

line 22, delete "II-2" and insert --9--.